UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,589	12/15/2003	Serengulam V. Govindan	328884	2607

35657 7590 06/20/2007

FAEGRE & BENSON LLP
PATENT DOCKETING
2200 WELLS FARGO CENTER
90 SOUTH SEVENTH STREET
MINNEAPOLIS, MN 55402-3901

EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
06/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/734,589	GOVINDAN, SERENGULAM V.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-8,10,13-15,17-34,36-45 and 48-66* is/are pending in the application.

4a) Of the above claim(s) *5-8 and 51-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,13-15,17,19,21-31,33,34,36,38,40-44,48-50 and 63-66* is/are rejected.

7)☒ Claim(s) *10,18,20,32,37,39 and 45* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/19/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/02/2007 has been entered.

Claims 1, 5-8, 10, 13-15, 17-34, 36-45, 48-66 are pending.

Claims 5-8 and 51-62 are withdrawn from consideration as being drawn to a non-elected inventions.

Claims 1, 10, 13-15, 17-34, 36-45, 48-50 and 63-66 are currently under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed on 3/19/2007 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-26, 44 and 63-66 remain rejection under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is apparent that the recited monoclonal antibodies are required to practice the claimed invention, because they are specifically required in the claims. As required elements they must be

known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the cell lines listed in claim 7. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining the monoclonal antibodies and they do not appear to be readily available material. Deposit of the hybridoma would satisfy the enablement requirements of 35 U.S.C. 112. While the specification states on page 5 that the cell lines "have been deposited for patent purposes", the specification does not indicate the terms of the deposit.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;
(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;
(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and
(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

In response to this rejection, Applicants assert, in short, that the Patent Office's reliance on Ex Parte Humphreys to reject claims drawn to monoclonal antibodies of known sequences is misplaced. In particular, Applicants assert that in contrast to Humphreys, there is no requirement for mutagenesis to produce the recited antibodies; and further, the sequences of the antibody variable regions were known in the art as of the instant priority date, as summarized in the amendment and response dated November 16, 2006. As such, Applicants assert that there is no requirement for undue experimentation in producing antibodies comprising such known sequences. Moreover, Applicants assert that at least the deposits of hybridomas encoding LL2 (ATCC PTA-6735), G250 (2526), CC49 (ATCC HB 9459, HB 12126) and L243 (ATCC HB55), as discussed in the response and amendment of November 16, 2006, were made under the terms of the Budapest Treaty and all restrictions imposed by the depositor will be irrevocably removed upon granting of a patent.

These arguments have been carefully considered, but are not found persuasive.

In response to Applicants assertions pertaining to Ex Parte Humphreys, the Examiner acknowledges Applicants analysis of Ex Parte Humphreys and conclusion that the instant case is not related. However, it is the Examiner's opinion that the issues involved in the instant case are related to those of Ex Parte Humphreys as stated above. For example, the Examiner recognizes that very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3rd ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibodies unless a deposit of the hybridoma is made. Similarly, regarding Applicants assertion that the deposit of the hybridomas encoding LL2 (ATCC PTA-6735), G250 (2526), CC49 (ATCC HB 9459, HB 12126) and L243 (ATCC HB55), as discussed in the response and amendment of November 16, 2006, were made under the terms of the Budapest Treaty and all restrictions imposed by the depositor will be irrevocably removed upon granting of a patent, the Examiner has carefully reviewed the previous response but can not find any reference to Applicants assertions that the hybridomas were deposited

under the terms of the Budapest Treaty. Lastly, the Examiner acknowledges that the hybridomas listed above have been referenced in each patent as being deposited (see response filed November 16, 2006). However, the Examiner recognizes that each case is different and the deposit of such material needs to be perfected in the application under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 13-15, 17, 19, 21-24, 27-31, 33-34, 36, 38, 40-43 and 48-50 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chari et al. (WO 01/24763 A2, 2001) in view of Zhao et al. (US 6,716,821, 2004).

Chari et al teach (page 2, lines 11-14 and page 5, lines 30-31) an immunoconjugate comprising a cell binding agent and at least one therapeutic agent for killing a selected cell population, wherein the cell binding agent is a monoclonal antibody or fragment thereof (i.e. Fv, Fab, Fab' and $F(ab')_2$) and the therapeutic agent is an anti-mitotic agent that is linked to the antibody via a linking group. With regards to the antibody, the WO publication teaches (page 17, lines 3-5) that the choice of the appropriate antibody depends on the cell population that is to be targeted. For example, Chari et al. teach (page 17, lines 6-13) that the monoclonal antibody anti-B4, which

binds to the CD19 antigen on B cells, can be used to target B cells. Alternatively, the WO publication teaches (page 17, lines 23-31) that antibody or fragment thereof that is specific for lung cancer such as an antibody that binds to an epitope on the CD56 antigen expressed on small cell lung cancers. With regards to the linking group, Chari et al. teach (page 6, lines 1-2) that suitable linking groups include, but are not limited to, esterase labile groups. Moreover, the WO publication teaches (page 6, lines 4-14, page 7, lines 1-5, page 9, formula II and/or III and page 21, lines 28-30) that the linking group is part of a chemical moiety having a peptide such as N-methyl-cysteine or N-methyl-alanine, covalently bound at the C-terminus to an anti-mitotic agent, such as a maytansinoid derivative, via an ester linkage, e.g., alpha carboxylic acid, and at the N-terminus to the cell-binding agent via a disulfide bond. As a result, the WO publication teaches (page 22, lines 1-2) the conjugates would have 1 to 10 drug molecules per antibody molecule. Moreover, Chari et al. teach (page 30, lines 9-22) that the immunoconjugates may be administered in a suitable form via i.v.. Thus, while Chari et al. do not characterize an antibody specific for an antigen expressed on small cell lung cancer as an antibody specific for an antigen expressed on a carcinoma cell, the claimed functional limitation would be an inherent property because as evidenced by Dictionary.com (see attached), small cell lung cancer is also referred to as small-cell lung carcinoma. Moreover, although Chari et al. does not specifically recite that the immunoconjugate is formulated for parental administration, the claimed functional limitation would be an inherent property because as evidenced by Stedman's Medical Dictionary (see attached), the term parental refers to the introduction of substances to an organism by intravenous, subcutaneous, intramuscular, or intramedullary injection. Thus, the claimed immunoconjugate appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Chari et al. do not explicitly teach that the linker further comprises a water-solubilizing moiety between the therapeutic moiety and the cell binding agent, wherein the water-solubilizing agent is an aminopolycarboxylate such as PEG. Nor does Chari et al. explicitly teach that the anti-

mitotic agent is a taxane, doxorubicin and/or analog thereof, or camptothecin, e.g. CPT, and/or analog thereof.

Zhao et al. teach that cytotoxic conjugates comprising a cytotoxic agent linked to a cell-binding agent via disulfide bonds or short disulfide containing linkers are only sparingly soluble in pharmaceutical solutions typically used for parental administration (column 1, lines 60-65). As a way to circumvent this technical difficulty, Zhao et al. teach cytotoxic agents bearing a polyethylene glycol (PEG) linking group having a terminal active ester and cytotoxic conjugates comprising one or more cytotoxic agents linked to a cell-binding agent via a PEG linking group (column 2, lines 51-57). With regards to the cytotoxic agents, the patent teaches that cytotoxic agents include, but are not limited to, maytansinoids, taxane, daunorubicin analogues and doxorubicin analogues (column 4, lines 1-5). With regards to the cell-biding agents, the patent teaches that cell-binding agents include, but are not limited to, antibodies, interferons, lymphokines, hormones and growth factors (column 64, lines 35-44). Specifically, the patent teaches that the antibodies include, monoclonal antibodies such as My9 and anti-B-4 which binds to a CD19 antigen.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to incorporate a water soluble moiety into the immunoconjugate taught by Chari et al in view of the teachings of Zhao et al.. One would have been motivated to do so because Zhao et al. teach that water solubility is one of the many technical difficulties relating to parental administration of cytotoxic conjugates. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by incorporating a water soluble moiety into the immunoconjugate taught by Chari et al in view of the teachings of Zhao et al., one would achieve a way of overcoming poor water solubility and increasing the antibodies efficiency.

Moreover, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute maytansinoids for taxane's and/or doxorubicin as the therapeutic agent of Chari's immunoconjugate. One would have been motivated to do so because each of the agents have been individually taught in the prior art to be therapeutic agents. The instant situation is amenable to the type of analysis set forth in In re Kerkhoven,205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to for a third composition that is to be used for the very same purpose since the idea of combining them flows

logically from their having been individually taught in the prior art. Applying the same logic to the instant claims, one of ordinary skill in the art would have a reasonable expectation of success that by substituting art recognized therapeutic agents such as taxane derivatives and/or doxorubicin analogues for the maytansinoid derivative taught by Chari et al., one would achieve an immunoconjugate effective for the specific delivery and treatment of cancer..

Claims 25 and 44 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chari et al. (WO 01/24763 A2, 2001) in view of Zhao et al. (US 6,716,821, 2004) in further view of Newton et al. (Blood 2001; 97: 528-535).

Chari et al in view of Zhao et al. teach, as applied to claims 1-4, 9, 11-15, 17, 19, 21-24, 27-31, 33-34, 36, 38, 40-43 and 48-50 above, an immunoconjugate comprising a cell binding agent and at least one therapeutic agent for killing a selected cell population, wherein the conjugate comprises a water soluble PEG linking group and the cell binding agent is a monoclonal antibody or fragment thereof (i.e. Fv, Fab, Fab' and $F(ab')_2$) and the therapeutic agent is an anti-mitotic agent that is linked to the antibody via a linking group. With regards to the antibody, the WO publication teaches (page 17, lines 3-5) that the choice of the appropriate antibody depends on the cell population that is to be targeted. For example, Chari et al. teach (page 17, lines 6-13) that the monoclonal antibody anti-B4 which is a murine IgG1, that binds to the CD19 antigen on B cells can be used to target B cells. Alternatively, the WO publication teaches (page 17, lines 23-31) that antibody or fragment thereof that is specific for lung cancer such as an antibody that binds to an epitope on the CD56 antigen expressed on small cell lung cancers.

Chari et al in view of Zhao et al do not explicitly teach that the targeting moiety is the antibody LL2.

Newton et al. teach (abstract) an immunoconjugate comprising LL2 covalently linked to the ribonuclease, onconase, wherein LL2 is an anti-CD22 monoclonal antibody against B-cell lymphoma.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the immunoconjugate as taught by Chari et al. in view of Zhao et al. with a monoclonal LL2 antibody in view of the teachings of Newton et al.. One would have been motivated to do so because as taught by Newton et al., the murine anti-CD22 monoclonal antibody

(LL2) was developed for imaging and treatment of non-Hodgkin B-cell lymphomas (NHL). Thus, one of ordinary skill in the art would have a reasonable expectation of success that by incorporating LL2 into the immunoconjugate of Chari in view of the teachings of Newton, one would achieve an immunoconjugate which comprises a targeting agent specific for Non-Hodgkin B-cell lymphomas.

In response to the previous rejection of the claims under 35 U.S.C. 103(a) as being unpatentable over Chari et al. (WO 01/24763 A2, 2001) in view of Zhao et al. (US 6,716,821, 2004), and under 35 U.S.C. 103(a) as being unpatentable over Chari et al in view of Zhao et al. in further view of Newton, Applicants assert that neither Chari nor Zhao, either alone or in combination, disclose all of the elements of the amended claims. For example, Applicants submit that the element of " a linker comprising a thiol-reactive functional group that binds to a thiol group on the antibody" is not disclosed. In particular, Applicants submit that this limitation is not taught by Chari et al. because in Chari the orientation of the bond is reversed and the thiol reactive group is on the antibody. Furthermore, Applicants assert that, in Chari et al., the bond occurs between the antibody and a thiol-containing anti-mitotic drug, wherein the use of a thiol containing drug for antibody conjugation has the disadvantage of possible cleavage of disulfide bonds within the antibody that are important for maintaining the antibody structure. Moreover, Applicants assert that another disadvantage is that thiol-containing agents can for aggregates which requires an additional step in purification. Secondly, Applicants assert that in contrast to Chari et al. the amended claims recite that the ester bond is between the chemotherapeutic moiety and a natural α-amino acid and not between the antimitotic drug and a carboxylic acid derivative that are not naturally occurring amino acids as taught by Chari et al. Finally, Applicants assert that the disclosure of Chari is fundamentally different and teaches away from the instant claimed subject matter because Chari et al. discloses a combination therapy using an immunoconjugate and, separately, a therapeutic agent. In contrast, Applicants assert that the instant claims recite an antibody linked to a therapeutic agent to form an immunoconjugate. With respect to the reference of Newton, Applicants assert that the reference is merely cited by the Action as merely disclosing "an immunoconjugate comprising LL2 covalently linked to the ribonuclease, onconase, wherein LL2 is an anti-CD22 monoclonal antibody against B-cell lymphoma. However, Applicants assert that there is no citation to Newton disclosing anything relating to "a linker comprising (i) a thiol reactive functional group that binds to a thiol group of the antibody, and (ii) a water solubilizing moiety, wherein the chemotherapeutic agent is

attached to the linker via an intracellular-cleavable moiety that is cleavable by intracellular esterases and comprises an ester formed from the a-carboxylic acid of an amino acid.

These arguments have been carefully considered but have not been found persuasive for the reasons set forth below.

First, regarding Applicants assertions with respect to the claims 1st limitation, the Examiner acknowledges that Chari et al. does not specifically teach " a linker comprising a thiol-reactive functional group that binds to a thiol group on the antibody". However, the Examiner recognizes that the instant claims are not drawn to a method of producing said conjugate, wherein the limitation of a "thiol-reactive functional group that binds to a thiol group of the antibody" would be an issue, but are drawn to the product, e.g., an immunoconjugate comprising. In other words, the Examiner recognizes that the claims are drawn to an immunoconjugate comprising: (a) an antibody; (b) a chemotherapeutic agent; and (c) a linker, wherein the linker is attached to the chemotherapeutic agent via an ester from the α-carboxylic acid of an amino acid and is attached to a thiol group on the antibody. As such, Chari et al. teachings of an immunoconjugate comprising: an antibody, a chemotherapeutic agent, and a linker which is attached to the chemotherapeutic agent via the a-carboxylic acid of an amino acid (see formula II page 9) and attached to the antibody via a disulfide bond anticipates the instantly claimed immunoconjugate. Secondly, regarding Applicants assertions that the reference fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., *natural amino acid*) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Lastly, with respect to Applicants assertions that Chari is fundamentally different from the instant invention, the Examiner acknowledges that Chari contemplates a combination therapy using an immunoconjugate and, separately, a therapeutic agent. However, the Examiner recognizes that the claims are drawn to the immunoconjugate, which is taught by Chari et al. and not to its therapeutic use. With regards to Applicants arguments pertaining to Newton et al., the Examiner acknowledges that Newton does not explicitly teach "a linker comprising (i) a thiol reactive functional group that binds to a thiol group of the antibody, and (ii) a water solubilizing moiety, wherein the chemotherapeutic agent is attached to the linker via an intracellular-cleavable moiety that is cleavable by intracellular esterases and comprises an ester formed from the a-carboxylic acid of an amino acid. However, the

Examiner recognizes that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

Claims 10, 18, 20, 32, 37, 39 and 45 appear to be free of the prior art, but are objected to as being dependent from a rejected independent claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

BF

6/7/2007